REMARKS

Applicant has thoroughly reviewed the outstanding Office Action including the Examiner's remarks and the references cited therein. The following remarks are believed to be fully responsive to the office Action, and when coupled with the above amendments, are believe to render all the claims at issue patentably distinguishable over the cited references.

Claims 6 and 14 are amended. Accordingly, claims 1-6, 8-14 and 16-19 are now pending in this application.

Telephone Interview Summary

The Applicant would like to thank the Examiner for participating in a telephone interview on December 11, 2007. In the telephone interview, the content of this Amendment After Final was proposed to the Examiner, and after discussion, the Examiner indicated that the proposed amendments and arguments would place the application in condition for allowance. This Amendment After Final reflects the amendments and arguments that were proposed, and a Notice of Allowance is therefore respectfully requested.

Claim Rejections – 35 U.S.C. § 112

The Examiner rejected claims 6 and 14 under 35 U.S.C. § 112, second paragraph, for the phrase "such as" has rendered the claim indefinite. Applicant has amended claims 6 and 14 in a manner responsive to the Examiner's concerns. Accordingly, Applicant respectfully submits that the Section 112 rejection has been overcome.

Claim Rejections - 35 U.S.C. § 102

The Examiner rejected claims 1-3 under 35 U.S.C 102(b) as being anticipated by Bodor et al., (Acta Pharma Nord. 1989, 1(4), 185-193). Applicants respectfully traverse this rejection as applied to claims 1-3 based on the reasons that Bodor et al. do not anticipate claims 1-3 of this application.

The Examiner has contended in the first Office Action and again in the final Office Action that the method of creating a drug-containing aqueous solution disclosed by Bodor et al. is similar to the method disclosed in Example 5 of the present application, and that since Example 5 produces a niosome, the Bodor et al. method must also produce a niosome.

It is respectfully submitted that the method disclosed by Bodor et al. is **not** similar to the method disclosed in Example 5, and does not produce a niosome. Bodor et al. teach mixing 2-hydroxypropyl- ß-cyclodextrin (2-HPCD) with 17 ß-estradiol by sonicating for an hour, then allowing the mixed solution to equilibrate in the dark for 48 hrs before diluting it with 50% methanol then measured drug concentration by reverse-phase HPLC methods (See page 186, the second paragraph of Bodor et al.). It is clear from the text provided in Bodor et al. that methanol was used not as a surfactant, but as a thinner or a dilutant. Therefore, the procedures described by Bodor et al. at best produce a cyclodextrin complex with estradiol, however, they **do not** produce a niosome as contended by the Examiner. One skilled in the art who follows the procedures described by Bodor et al. **would not** obtain **the niosome of instant claim 1,** which comprises within its structure a cyclodextrin inclusion complex of an active compound, and a non-ionic surfactant vesicle. Merely adding methanol to a mixture of cyclodextrin and a steroid compound does not produce a niosome. Furthermore, the alcohol type of non-ionic surfactants suitable for forming a niosome are fatty alcohols such as those described in lines 2-5, page 9 of the specification, and one skilled in the art knows that methanol is not a proper choice for non-ionic surfactant.

By contrast, the method disclosed in Example 5 of the specification involves rapid addition of a non-ionic surfactant-containing ethanol solution to a hot water solution, and removal of a solvent of the mixed solution by reduced pressure concentration, followed by freeze-drying and/or spray-drying to generate niosomes. The niosome powders are rehydrated for use. The method taught by Bodor et al. on page 186, paragraph 2, is not similar to this method, as it involves adding a drug to an aqueous solution containing 2-HPCD (but not including a non-ionic surfactant), and then diluting the solution with aqueous methanol. There is no disclosure in the Bodor et al. publication that this method produces a niosome, and the significant differences between this method and the method

disclosed in Example 5 of the specification would not lead one skilled in the art to believe that the Bodor et al. method would produce a niosome (and in fact, the method would not produce a niosome).

In view of the above, Bodor et al. at best generate a cyclodextrin complex with a steroid compound, but they do not produce a niosome, let alone the niosome of this instant claim 1. In other words, Bodorr et al. do not identically disclose or describe this invention, and Applicant respectfully requests that §102(b) prior art rejection be withdrawn.

The Examiner further rejected claim 19 under 35 U.S.C 102(b) as being anticipated by Bodor et al., (Acta Pharma Nord. 1989, 1(4), 185-193). Applicants respectfully traverse this rejection as applied to claim 19 based on the reasons that Bodor et al. do not anticipate claim 19 of this application.

Claim 19 is directed to a method for facilitating transdermal delivery of a steroidal active agent, comprising the step of administering to a human or an animal the composition of claim 1. As explained above, Bodor et al. do not teach or suggest the composition of claim 1, nor do them teach or suggest the use of the novel composition of claim 1 of this invention. In other words, Bodor et al. do not identically disclose claim 19, nor is any person skilled in the art capable of conceiving the idea of claim 19 of this invention in view of Bodor et al. Applicant respectfully requests this lack of novelty rejection of claim 19 over Bodor et al. be withdrawn.

Claim Rejections - 35 U.S.C. § 103

The Examiner rejected claims 4-6 and 8 under 35 U.S.C. 103(a) as being unpatentable over Bodor et al., (Acta Pharma Nord. 1989, 1(4), 185-193) in view of Siguroardottir et al. (Drug Development and Industrial Pharmacy, 1994, 20(9), 1699-1078) and newly cited Heiber et al. (US 5,212,199). Applicant respectfully traverses this rejection as applied to claims 4-6 and 8 on the basis that the art cited by the Examiner, either alone or in combination, fails to teach or suggest the claimed invention.

The differences between the teachings of Bodor et al. and that of this instant invention have been fully explained as above. In short, the procedures described by Bodor et al. do not produce a niosome, let alone the niosome of instant claim 1.

As to Siguroardottir et al., Applicant has pointed out in the previous responding statement that what Siguroardottir et al. did was using HPßCD to release drug from a topical vehicle system such as oil-in-water cream system like Uniderm® 1% cream vehicle system, and glyceryl monostearate was just one of the many constituents of the oil cream system. In other words, no niosome was ever produced in Siguroardottir et al.'s studies, nor was there any text suggested or taught about producing the niosome of instant claim 1, which comprises within its structure a cyclodextrin inclusion complex of an active drug, and a vehicle formed by nonionic surfactant. Neither is there any description in Siguroardottir et al. that their work is drawn to a composition similar to Bodor et al. as indicated by the Examiner. In fact, Applicant believes that the teaching provided by Siguroardottir et al. is un-related to this instant invention, nor is it related to Bodor et al.

As to the newly cited Heiber et al., they described a skin permeation enhancer composition comprising an active drug and a permeation enhancer composition, which consists essentially of: (1) a sorbitan ester; or (2) a sorbitan ester in combination with an aliphatic alcohol. The procedure described by Heiber et al. is well known, so is the drawback of their method. The major problem in Heiber et al.'s method is that by using a surfactant as a permeation enhance of a steroid compound, often times the active drug (such as estriol) stops at the corneum layer, instead of crossing the corneum and reach the dermal layer of a skin. To overcome this problem, Applicant found out that if the active drug is first included in the cyclodextrin complex, then forms a niosome with a nonionic surfactant, the niosomes thus formed would be able to carry the active compound across the corneum layer and reach the dermal layer of a skin, and therefore would greatly enhance the efficacy of the active compound. Again, nowhere in Heiber et al. had they suggested or taught a composition of this instant claim 1.

None of the references of record disclose, teach or suggest the niosome composition recited in claim 1, either alone or in combination. Claims 4-6 and 8 are therefore patentable over

Bodor et al. (Acta Pharma Nord. 1989, 1(4), 185-193) in view of Siguroardottir et al. (Drug Development and Industrial Pharmacy, 1994, 20(9), 1699-1078) and newly cited Heiber et al. (US 5,212,199).

The Examiner further rejected claims 9-18 under 35 U.S.C. 103(a) as being unpatentable over Bodor et al., (Acta Pharma Nord. 1989, 1(4), 185-193) in view of Loftsson (US 5,472,954) and newly cited Heiber et al. (US 5,212,199). Applicant respectfully transverses this rejection as applied to claims 9-18 on the basis that the art cited by the Examiner, either alone or in combination, fails to teach or suggest the claimed invention.

The teachings of Bodor et al. and Heiber et al., and the differences between these two references and this instant invention have been fully explained as above.

Regarding the teachings provided by Loftsson, as Applicant has pointed out in previous response, similar to the method described by Bodor et al., Loftsson merely teaches a method of forming a complex of cyclodextrin and a water-liable active compound. No where in Loftsson had he taught or suggested forming a cyclodextrin inclusion complex with an active drug first, then mixing this active drug included cyclodextrin complex with a nonionic surfactant to form a niosome in accordance with the steps of this instant claim 9. Further, none of the cited references has taught or suggested combining the teaching of Bodor et al. or Loftsson and the surfactants of Heiber et al. in obtaining this instant claim 9. Therefore, Applicant respectfully submits that claims 9-18 are patentable over Bodor et al. (Acta Pharma Nord. 1989, 1(4), 185-193) in view of Loftsson (US 5,472,954) and Heiber et al. (US 5,212,199).

CONCLUSION

In view of the foregoing amendments and remarks, Applicant believes that all the pending claims as amended herein are distinguishable from the cited prior art, and the Examiner is respectfully requested to enter the requested amendments and to pass this application for allowance.

The amendments made herein are responsive to the Examiner's suggestions for correcting the form of the claims, and therefore are proper for entry after final rejection under 37 C.F.R. 1.116.

Respectfully submitted,

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By: _____

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